

# CHARACTERIZATION OF AUTONOMIC NERVOUS INFLUENCES ON PR AND RR INTERVALS IN THE ELECTROCARDIOGRAM

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**Abstract-** RR and PR intervals were extracted from single channel electrocardiograms in normal human subjects using a wavelet based technique. RR and PR intervals were shown to be correlated with respiration due to common autonomic nervous activation of the sino-atrial and atrio-ventricular nodes. However, evidence for independent autonomic nervous activation of these nodes is also shown based on RR and PR interval spectra, and on RR vs. PR plots.

**Keywords -** Electrocardiogram, autonomic nervous system, PR interval, RR interval, respiration, heart rate variability

## I. INTRODUCTION

Heart rate variability (HRV) has been extensively studied in recent years. Changes in the parameters of HRV have been linked with pathologies such as congestive heart failure and atrial fibrillation, and it is hypothesized that underlying changes in autonomic nervous system (ANS) activity are reflected in HRV. Previous studies of HRV, and by extension the underlying ANS activity, have concentrated on analysis of HRV based on measurement of RR intervals (the times between QRS complexes). In this paper, we also consider variability in the PR interval (defined as the time between the onset of the P-wave, and QRS onset), as an additional useful measure of ANS activity affecting the heart. It is already well known that ANS activity can affect conduction time through the atrio-ventricular node, and hence affect the PR interval. This paper shows how respiration can modulate PR interval length, and also that independent modulation of the PR and RR intervals occurs under normal physiological circumstances.

## II. BACKGROUND PHYSIOLOGY

Under normal physiological conditions, the heartbeat is initiated by spontaneously generated action potentials at the sinoatrial (SA) node. When the SA node fires, a wave of depolarization propagates through the atrial myocardial cells causing atrial contractions. This depolarization can be detected on the skin surface as the P-wave of the ECG. Hence, the onset of the P-wave is the best indicator available of the time of firing of the SA node. The wave of atrial depolarization is directed along the interventricular septum. Here the atrio-ventricular (AV) node slows conduction to produce a physiologic delay whose purpose is to allow the atria to finish contracting before the ventricles begin to contract. The QRS complex is primarily associated with ventricular depolarisation; hence the onset of the QRS complex marks the point when electrical activity leaves the AV node. The PR interval (time from the onset of the P-wave until the onset of the QRS complex) is taken as a common

measure of conduction delay in the AV node. An underlying assumption for this is that the time of conduction from the SA to AV nodes is reasonably fixed under normal physiological conditions.

The body can regulate two processes; firstly, the overall cycle length and hence heart rate, and secondly the speed of conduction of the electrical activity through the heart including the AV node. The exact physiological purpose of the second mechanism is not yet fully elucidated, though a reasonable hypothesis is that it acts to minimize the likelihood of arrhythmias.

The autonomic nervous system (ANS) is the primary controller for both overall cycle length and AV conduction delay. Changes in cycle length or AV conduction delay usually involve a reciprocal action of the two divisions of the ANS. Shortened cycle lengths or AV conduction delays are produced by a diminution of parasympathetic and simultaneous increase in sympathetic activity. Increased cycle lengths or AV conduction delays are usually achieved by the opposite mechanism [1]. In addition, AV conduction delay is also influenced by refractory effects. Encroachment upon the relative refractory period of the AV node will have the paradoxical effect of lengthening AV conduction time as cycle length shortens.

It is not fully established whether independent autonomic control of cycle length and AV conduction delay is apparent under normal physiological circumstances, and an aim of our study is to investigate this question. In other words, does the autonomic nervous system induce independent variation of RR and PR interval duration under normal physiological conditions?

It is certainly physiologically plausible that independent autonomic modulation of cycle length and AV conduction time can occur. Parasympathetic innervation for both the SA and AV nodes originates in the cardiac inhibitory center in the medulla and is conveyed to the heart by way of the vagus nerve. However, the SA node is predominantly affected by the right vagus nerve, whereas the AV node is predominantly driven from the left vagus. Normal parasympathetic innervation represents the dominant neural influence on the heart. The ANS is itself operating in response to various factors. In particular two of the strongest factors influencing the ANS are respiration and blood pressure, hence variations in these can be viewed indirectly as primary sources of HRV. Respiratory sinus arrhythmia (RSA) is rhythmical fluctuations in RR interval characterized by a decrease in the

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RR interval length during inspiration and an increase in the RR interval length during expiration. The underlying physiological hypothesis for RSA is that the vagus nerves are inhibited during inspiration and excited during expiration while the sympathetic nerves are thought to be excited during inspiration and inhibited during expiration. However the latter effect is low pass-filtered at the heart and has a minimal impact on RSA. RSA is particularly well pronounced in younger subjects, and when a person is supine.

The baroreflex can also modulate ANS activation, and hence heart rate. A baroreflex occurs in response to a decrease in blood pressure (e.g., when standing up) which is sensed by the baroreceptors. These produce an increase in sympathetic activity and a decrease in parasympathetic activity. This results in an increase in heart rate and helps to restore blood pressure to normal levels.

If the overall ANS activity driving the SA and AV nodes is tightly coupled (i.e., there is little independent modulation), then a close analogue of RSA should be seen in the PR interval variability. Hence, one of our initial investigations was to determine the correlations between respiration, RR intervals, and PR intervals. RSA is particularly pronounced when a person is at rest and breathing deeply, which is why periods of deep breathing were included in the data acquisition protocol.

### III. DATA ACQUISITION

In order to determine the relation between cycle length and AV conduction time, and to consider the effect of respiration on both, data was collected from normal healthy subjects. The data consisted of single lead ECG signals of 70-minute duration recorded using the Lewis lead electrode configuration with disposable silver-silver chloride electrodes (Table 1). Signals were amplified, bandpass filtered (0.1-100Hz) and digitised at a sampling rate of 1000 Hz using the Biopac (Biopac Systems Inc. California). Respiration was monitored simultaneously by measuring chest wall volume using a calibrated respiratory inductance plethysmograph (Respirace, Ambulatory Monitoring, Ardsley, NY). To consider the effect of different body postures, signals were recorded in three different positions: supine, standing and sitting. Subjects also performed two standard tests of cardiac autonomic responsiveness: two minutes of deep breathing, and the Valsalva manoeuvre. The Valsalva manoeuvre raises blood pressure and hence stimulates vagal input to the heart. Table 1 gives a summary of the data acquisition protocol.

### IV. TIMING INTERVAL EXTRACTION

Automated analysis of the ECG and extraction of timing information of interest such as P-wave onset, QRS onset, and

TABLE 1  
DATA COLLECTION PROTOCOL

Time (s)	Procedure
0	Start recording supine resting ECG
1200	2 mins deep breathing (5 seconds in, 5 seconds out)
1320	End deep breathing, remain supine
1800	Stand
2400	2 mins deep breathing (5 seconds in, 5 seconds out)
2520	End deep breathing, remain standing
3000	Sit
3600	Valsalva maneuver (15 s, 40 mmHg)
3900	Valsalva maneuver (15 s, 40 mmHg)
4200	End

PR duration has been extensively studied in the literature. In this work, the parameters of interest are RR interval, PR interval, and respiration, so ECG processing is aimed at reliable extraction of the first two of these. This task can be considered as QRS and P-wave detection, followed by accurate measurement of the onset of these events. The method used in this paper is fully described by Sahambi *et al.* [2]. Slight modification was needed to account for the fact that our database contained Lewis lead recordings rather than the Lead II recordings used in their work.

The technique uses the wavelet transform to identify transient events such as the QRS complex and P-wave, since the energy contained in these events is spread across multiple scales. Specifically, it is well known that a discontinuity in a signal leads to maxima in the magnitude of the Discrete Wavelet Transform (DWT) across different scales. By tracking pairs of maxima across different scales, it is possible to accurately locate QRS complexes and P waves. The onset points were estimated by searching backwards from the QRS peaks or P wave peaks until the magnitude of the wavelet transform had fallen below an empirically determined threshold. The wavelet used in this study was the negative derivative of a Gaussian function:

$$y(t) = -C \frac{d}{dt} \exp(-t^2). \quad (1)$$

Based on identification of the P onset, the QRS onset, and the R-wave peak, the PR and RR intervals were calculated.

The automated method for PR and RR interval measurement was validated in two ways. Firstly, the overall accuracy of QRS and P wave detection was estimated by comparing QRS complexes and P waves detected by an expert human observer with those produced by the automated technique. The overall error rate for QRS detection was 0.22%, and that for P-wave detection was 0.11%. The error rate was defined as the sum of missed events plus spurious events divided by the total number of events. These figures are comparable with other results in the field. A second validation was to estimate the precision of the measured RR and PR intervals, since the definition of onset is somewhat arbitrary. To do this a random selection of 60 beats (chosen from four subjects in each of the three positions) was manually annotated by an expert observer. The standard deviation of the difference between their markings and the

automated labeling of the onset times was calculated. For QRS complex onset, the standard deviation was approximately 4 ms, whereas for P wave detection it was approximately 2.5 ms. These figures mean that it is reasonable to consider variations of PR and RR intervals greater than  $\pm 4$  ms, as done later in this paper.

## V. RESULTS

A first analysis was to estimate the influence of respiration on both the RR and PR interval lengths. Since respiration is a continuous function of time, we first derived rate functions from the RR and PR intervals. A signal  $RR(t)$  was constructed which was piecewise-constant between times  $R[i] - t_R/2$  and  $R[i+1] - t_R/2$ , where  $R[i]$  denotes the time at which the  $i^{\text{th}}$  R wave was detected and  $t_R$  denotes the mean RR interval spacing for that record. The value of the signal at these times was set to be  $1/(R[i+1] - R[i])$ . A signal  $PR(t)$  was defined in a similar fashion with  $PR(t) = 1/PR[i]$  for the times between  $R[i] - t_R/2$  and  $R[i+1] - t_R/2$ . The offsets were introduced so that the effect of an R or P wave would be spread over the time both before and after its detection. These signals were then correlated with the respiration signal  $V(t)$ .

The correlation coefficients were defined as:

$$C_{RR-V} = \frac{E[(RR(t) - \overline{RR(t)}) (V(t - \Delta t) - \overline{V(t)})]}{\sqrt{E[(RR(t) - \overline{RR(t)})^2] E[(V(t - \Delta t) - \overline{V(t)})^2]}} \quad (2)$$

$$C_{PR-V} = \frac{E[(PR(t) - \overline{PR(t)}) (V(t - \Delta t) - \overline{V(t)})]}{\sqrt{E[(PR(t) - \overline{PR(t)})^2] E[(V(t - \Delta t) - \overline{V(t)})^2]}} \quad (3)$$

where the overbar denotes averaging, and  $\Delta t$  is a delay factor. Because of the spreading in our rate function, and the fact that there is some delay between respiration and associated neural activity in the heart, we searched for the minimum correlation coefficient in a window of 5 s following  $V(t)$  (i.e.,  $\Delta t$  was set in the range 0–5 s). The minimum correlation coefficient was used, since rate is inversely related to interval length. Table 2 shows that significant correlation between respiration, RR interval, and PR interval was seen in both supine and standing positions, and that deep breathing increased the strength of this correlation

TABLE 2  
AVERAGE OBSERVED CORRELATION COEFFICIENTS  
BETWEEN RESPIRATION AND ECG INTERVALS

STATUS	$C_{RR-V}$	$C_{PR-V}$
SUPINE	-0.30	-0.27
SUPINE (DEEP BREATHING)	-0.81	-0.49
STANDING	-0.40	-0.30
STANDING (DEEP BREATHING)	-0.72	-0.34

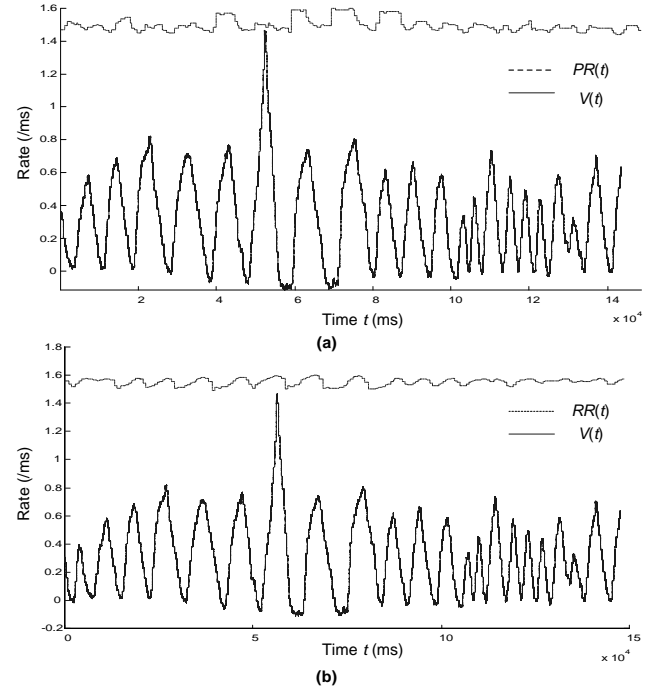


Figure 1: Correlation between respiration  $V(t)$ , PR, and RR intervals. In both panels, the upper trace is the rate function, shifted and scaled to appear on the same axis as  $V(t)$ . The lower trace is respiratory tidal volume  $V(t)$ . Panel (a) shows the correlation between respiration and the  $PR(t)$  function. Panel (b) shows the correlation between respiration and the  $RR(t)$  function

Figure 1 illustrates the degree of correlation between both RR and PR intervals, and respiration. These traces have not been time-shifted

If autonomic modulation of SA and AV nodes is tightly coupled, then it is reasonable to predict that the RR and PR interval spectra will be highly similar, with allowance for their different overall magnitudes. Figure 2 shows power spectral density estimates from two different subjects, in both the supine and standing positions (normal breathing). In each panel, the upper trace is the RR interval spectrum, and the lower is the PR interval spectrum. There are several comments that can be made about these spectra. Firstly, the RR and PR spectra are broadly similar, which supports the hypothesis that their modulation is tightly coupled. However, both subjects have a peak near 0.06 cycles/interval (approximately equivalent to 0.1 Hz) in the RR interval spectrum when standing. This peak can probably be attributed to a baroreflex response [3]. However, for one subject (PAN230302), this peak is absent in the PR interval spectrum, whereas for the other (PAN040402) it is clearly present in the PR interval spectrum. An interpretation is that in different subjects (or perhaps even in the same subject at different times), there is some degree of independent SA and AV modulation.

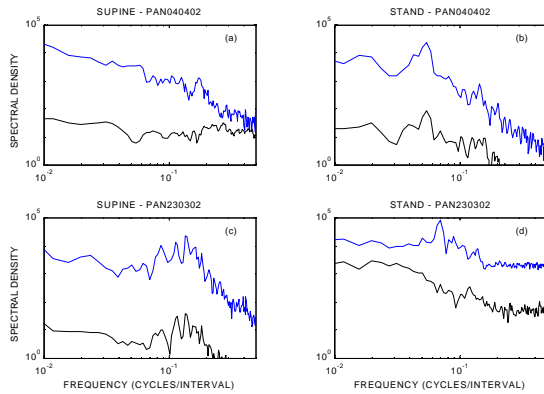


Figure 2: PR and RR interval spectra for two subjects in both the supine and standing position. Panels (a) and (c) show the subjects in the supine position, and (b) and (d) are for standing. In Panel (b) a peak at 0.05 cycles/interval is apparent in both RR and PR spectra; in Panel (d) a similar peak only occurs in the RR interval spectrum.

Furthermore, assuming that the AV node and the SA node share a tightly coupled autonomic modulation, then the same RR interval should always be associated with approximately the same PR interval. Figure 3 plots RR vs. PR for one subject in both the supine and standing position. The crosses denote the relation in the supine position, while the circles are for standing. In general, for this subject, for the same RR interval, there is a significantly shorter PR interval when standing than when lying down. This behavior is seen in approximately 50% of the subjects studied. A reasonable explanation is that the independent modulation of SA and AV nodes is taking place. Other factors such as changes in the sensitivity of the SA and AV nodes to ANS activity cannot be ruled out, but seem more physiologically unreasonable. The transition from the "supine" to the "standing" regime takes approximately 15 beats, and so can probably be attributed to increased sympathetic activity in the AV node not present in the SA node.

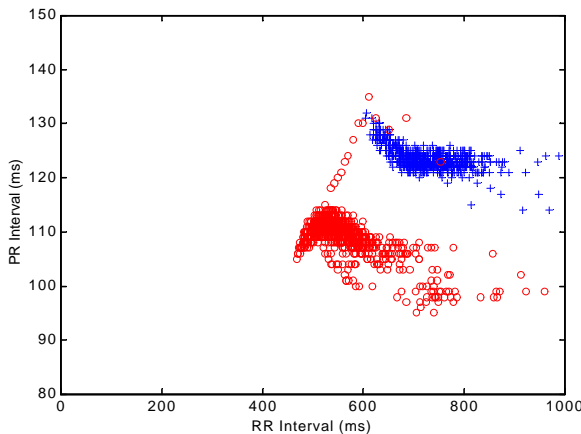


Figure 3: Preceding RR interval vs. PR interval for one subject in both the supine and standing position (o = standing, + = supine).

#### IV. DISCUSSION AND CONCLUSION

We have presented a technique for measurement and analysis of respiration, PR intervals, and RR intervals in normal human subjects. The technique for extraction of RR and PR timing is based on the wavelet transform and has been shown to have a low error rate (approx. 0.2%), and good precision (approx.  $\pm 4$  ms). Using this technique, we have carried out analysis on a database of recordings from seven subjects. We have shown that respiratory sinus arrhythmia can be seen in the PR intervals, though it is not as strong an effect as for RR intervals. This confirms the manual recordings carried out by Rawles *et al.* [4], which have not been subsequently verified by an automated method. Spectral analysis of the RR and PR intervals indicates that in general their variability is well correlated. However, in some subjects there is evidence for independent modulation of the RR interval and PR interval, since variability due to a baroreflex response is absent from the PR interval spectrum. Further evidence for independent modulation of PR and RR intervals is given by the fact that the same range of RR intervals can be associated with quite different PR intervals in different body positions. This effect is highly subject-dependent.

Other authors have also considered some of these issues. In [3], the authors tried to account for the rate-recovery effect in the AV node in order to isolate the autonomic-induced variability in RR and PR intervals. They concluded that in general the autonomic influence on the SA and AV nodes is tightly coupled. Kowallik and Meesmann [5] came to a different conclusion. By examining spontaneous changes in heart rate during sleep, they showed independent changes in RR and PR interval, even accounting for rate recovery effects. They concluded that independent modulation of the SA and AV nodes does occur under normal physiological conditions. Our results support their hypothesis.

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